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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,322	01/25/2000	Mich B. Hein	TSRI 184.2D1	8393

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	23

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/491,322	HEIN ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 February 2003* .

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,15-27 and 29-91* is/are pending in the application.

4a) Of the above claim(s) *66-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 15-27,29-65,83-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment filed February 19, 2003, paper no.22, has been entered.

Claims 13, 41 and 83 are newly amended.

Claims 13, 15-27 and 29-91 are pending.

Claims 66-82 are withdrawn from consideration.

Claims 13, 15-27, 29-65 and 83-91 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claim 29-30, 48-50 and 86-88 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

First, Applicants point out that the claims require an "antigen-specific immunoglobulin molecule" or immunologically active fragment, which means that the heavy chain must have a complete or nearly complete variable region, which typically constitutes about 100 amino acids, such that the claims would not read on a single amino acid (reply page 4). Second, Applicants

point to page 10 of the specification in support of claim language directed to a nucleotide sequence encoding an immunoglobulin heavy chain comprising "at least a portion" of a constant region. Applicants argue that the reference to "at least the immunologically active portion of an immunoglobulin heavy chain" is an implicit reference to heavy chain variable regions that have any number of constant region residues, and that any and all fragments were contemplated. Applicants also point to page 3 of the specification, and argue that the passage cited there indicates that recombinant expression makes possible the product of a variety of immunoglobulins, including those known from proteolytic processing as well as those known only by recombinant engineering. Applicants additionally argue that those skilled in the art would have appreciated that recombinant DNA methods could be used to produce immunoglobulins with heavy chains that include at least a portion of a light chain, and point to specific examples from the prior art as of the earliest filing date of the instant application (reply pages 4-5).

First, the relevance of Applicants' comment that the heavy chain must have a complete or nearly complete variable region, which typically constitutes about 100 amino acids, such that the claims would not read on a single amino acid, is unclear, as the claims recite "at least a portion of a heavy chain constant region". Second, the examples cited in the specification at pages 3 and 10 are directed to those antibody fragments that are known from proteolytic processing, rather than those produced only as a consequence of recombinant engineering. That it was known in the art that engineered immunoglobulins could be produced by recombinant DNA methods does not overcome the rejection, because such engineered immunoglobulins are neither disclosed nor exemplified in the specification. Accordingly, this rejection is being maintained.

Claim Rejections - 35 USC § 102

Claims 13, 15-27, 29-65 and 83-91 remain rejected under 35 U.S.C. 102(b) as being anticipated by Stolle et al. (US Patent No. 4,748,018), for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

With respect to the previous assertion by the Office that Applicants must demonstrate that the antibody produced in plants is different from that produce in chickens by Stolle et al, Applicants argue that all claim limitations must be considered when weighing the differences between the claimed invention and the prior art. Applicants also point out that the preamble of the independent claims has been further amended to emphasize the method by which the antibody is produced. Applicants argue that unless the Examiner takes the position that the claims at issue are something other than a method or process claim, she must acknowledge the materiality of the plant production limitation and withdraw the rejection. (reply pages 7-8).

The Office maintains that all claim limitations have been considered when weighing the differences between the claimed invention and the prior art. There is no evidence, however, that the requirement that the immunoglobulin be produced by transgenic plant cells is material with respect to distinguishing the claimed invention from that which is taught by the prior art. The limitations "produced by transgenic plant cells" and "obtained by processing plant cells" refer to the immunoglobulin and formulation products used in the claimed method. The method does not require producing immunoglobulins in transgenic plant cells, or obtaining formulation products by processing plant cells. Accordingly, absent evidence that the immunoglobulin used in the

claimed method is somehow different from the immunoglobulin used in the method taught by Stolle et al., the method taught by Stolle et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

Claims 13, 15-27 and 29-65 and 83-91 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (US Patent No. 4,956,282) and the During dissertation (Univ. of Koln, FRG, English translation, July 9, 1988) in view of Stolle et al. (US Patent No. 4,748,018), for the reasons of record set forth in the office action mailed November 19, 2002.

Applicant's arguments filed February 19, 2003, have been fully considered but they are not persuasive.

Applicants first argue that the rejection should be withdrawn because it is improperly based on a requirement that Applicants demonstrate that the antibody expressed in plants is different from the antibody of the prior art (reply pages 8-9).

As discussed *supra* under 35 U.S.C. 102(b), the Office maintains that the requirement that Applicants demonstrate that the antibody expressed in plants is different from the antibody of the prior art is not an improper requirement.

Second, Applicants argue that the rejection should be withdrawn because one skilled in the art would not have believed that During had successfully produced antigen-specific immunoglobulins in plants (reply pages 9-10).

The Office maintains that doubts about and criticism of the techniques employed by During in his experiments, such as those set forth in the Lerner declaration, does not overcome

the rejection, because the During reference nonetheless teaches the production of antibody molecules in plant cells.

Third, Applicants argue that the rejection should be withdrawn because it is based on the mistaken belief that the claims are not directed to a processed and fully assembled immunoglobulin. Applicants argue that the claims do not read on any and all fragments of a full-length antibody, but only on antigen-specific antibody fragments that have a two-chain structure. Applicants additionally point to the submitted declaration of Dr. Andrew Hiatt to demonstrate that an antigen-specific immunoglobulin fragment requires processing and assembly, as would the full-length fragment from which it is derived (reply page 10).

The Office acknowledges the declaration of Dr. Andrew Hiatt explaining the processing and assembly requirements for antigen-specific immunoglobulin fragments. The declaration does not, however, overcome the rejection, as the Office considers both the During and Goodman references to teach the production of antibodies in plant cells, notwithstanding the criticism set forth in the Lerner declaration.

Fourth, Applicants argue that the rejection should be withdrawn because it is based on the mistaken belief that the findings of the Lerner declaration are not commensurate in scope with the claims. Applicants again point the submitted declaration of Dr. Andrew Hiatt to demonstrate that an antigen-specific immunoglobulin fragment requires processing and assembly, as would the full-length fragment from which it is derived (reply page 11).

The Office acknowledges the declaration of Dr. Andrew Hiatt explaining the processing and assembly requirements for antigen-specific immunoglobulin fragments, and acknowledges that such requirements would place the antigen-specific immunoglobulin fragments of the instant invention within the scope of the concerns expressed in the Lerner declaration. The declaration does not, however, overcome the rejection, as the Office considers both the During and Goodman references to teach the production of antibodies in plant cells, notwithstanding the criticism set forth in the Lerner declaration.

Fifth, Applicants argue that the rejection should be withdrawn because there is no basis to support that the combination of cited art provides a reasonable expectation of success. Applicants argue that there is no basis to support that the combination of cited art provides a reasonable expectation of success because the During reference is not credible, because the Goodman reference is not enabled, and because in demonstrating only expression of interferon in plants Goodman cannot carry any weight in rendering the claims obvious (reply pages 11-12).

With respect to the credibility of the During reference, the Office maintains that the During reference teaches the production of antibody molecules in plant cells, notwithstanding the criticism set forth in the Lerner declaration. With respect to the Goodman reference, the Office maintains that Goodman need not exemplify antibody expression in order to be enabling, and that accordingly Goodman's teaching to express antibodies in plants does carry weight in rendering the claims obvious.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
May 19, 2003

PHUONG T BUI
PRIMARY EXAMINER 5/19/03